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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,511	06/30/2004	Stephen Francis Badylak	3220-72178	6418

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	
MAIL DATE	**DELIVERY MODE**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,511	BADYLAK ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-15 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4-25-08 has been entered.

Applicants' amendment filed 4-25-08 has been entered. Claim 11 has been amended. Claim 19 has been added. Claims 1-19 are pending. Claims 11-15 and 17-19 are under consideration.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 11-15 and 17-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The phrase "the DNA content of the liver basement membrane is about 0.566 to about 0.04 microgram of DNA per milligram of dry weight of the liver basement membrane" in claim 11 is considered new matter. Applicants point out support for the phrase is in Example 8, page

22, line 13, labeled "Native" of the specification. Example 8 on page 22 of the specification fails to provide any support for the DNA content from about 0.566 to about 0.04 microgram of DNA per milligram of dry weight of the liver basement membrane. The table only shows "average" and "standard deviation" of DNA content. No such range of DNA content can be found in Example 8. Thus, the phrase "the DNA content of the liver basement membrane is about 0.566 to about 0.04 microgram of DNA per milligram of dry weight of the liver basement membrane" is considered new matter. Claims 12-15, 17 and 18 depend from claim 11.

The phrase "the DNA content of the basement membrane is about 0.566 to about 0.04 microgram of DNA per milligram of dry weight of the basement membrane" in claim 19 is considered new matter. Applicants point out support for the phrase is on page 5, lines 30-33 and page 6, lines 14-17 of the specification. The cited pages 5 and 6 of the specification fails to provide any support for the DNA content from about 0.566 to about 0.04 microgram of DNA per milligram of dry weight of the basement membrane. Lines 30-33 of page 5 discuss collagenous structure of the liver basement membrane and the desire to minimize degradation of the membrane structure during cell dissociation. Lines 14-17 of page 6 disclose the use of protease and EDTA to optimize release and separation of cells from the basement membrane without substantial degradation of the membrane matrix. No such range of DNA content in any basement membrane can be found on pages 5 and 6. Thus, the phrase "the DNA content of the basement membrane is about 0.566 to about 0.04 microgram of DNA per milligram of dry weight of the basement membrane" is considered new matter.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Robinson et al., 1980 (European Journal of Biochemistry/FEBS, Vol. 111, No. 2, pp. 485-490).

Claim 19 is directed to a collagenous tissue graft structure comprising decellularized basement membrane wherein DNA content of the basement membrane is about 0.566 to about 0.04 ug/mg dry weight of the basement membrane.

Robinson teaches isolating basement membrane from rabbit kidney using detergent N-dodecyl sarcosine, the residual proteins were collagenous and the extracted membranes retained their continuity of structure and exhibited a matrix composed of fibrous and globular elements (e.g. abstract). Since the specification fails to disclose any basement membrane having the DNA content recited in the claim (see the new matter rejection set forth above), it appears that the claimed decellularized basement membrane is isolated from a subject without any exogenous modification. It is inherent that the kidney basement membrane isolated by Robinson contains the DNA content recited in the claim. Thus, claim 19 is anticipated by Robinson.

6. Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Brendel et al., 1980 (Advances in Experimental Medicine and Biology, Vol. 131, pp. 89-103).

Claim 19 is directed to a collagenous tissue graft structure comprising decellularized basement membrane wherein DNA content of the basement membrane is about 0.566 to about 0.04 ug/mg dry weight of the basement membrane.

Brendel teaches isolation of vascular basement membrane from several organs, such as kidney, lung, placenta and brain, via nondisruptive detergent solubilization techniques with detergent and DNase (e.g. p. 89, Table 1). The vascular basement membrane is decellularized and the remaining materials include basement membrane, interstitial collagen and a few other proteins such as fibrin, tubulin and actin (e.g. p. 91, 1st paragraph). Since the specification fails to disclose any basement membrane having the DNA content recited in the claim (see the new matter rejection set forth above), it appears that the claimed decellularized basement membrane is isolated from a subject without any exogenous modification. It is inherent that the vascular basement membrane isolated by Brendel contains the DNA content recited in the claim. Thus, claim 19 is anticipated by Brendel.

7. Claims 11-15 and 17-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Badylak, Stephen, 2002 (US Patent No. 6,379,710 B1, IDS-AG)

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the

inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 11-15, 17 and 18 are directed to a purified liver basement membrane graft composition comprising basement membrane of warm-blooded vertebrate liver tissue, wherein the DNA content of the liver basement membrane is about 0.566 to about 0.04 microgram of DNA per milligram of dry weight of the liver basement membrane, and wherein the liver basement membrane could be fluidized, in gel form, or in powder form, and a liver tissue derived composition for supporting the growth of a cell population, said composition comprising said liver basement membrane composition and is devoid of source liver tissue endogenous cells, or said composition comprising culture-ware coated with a matrix comprising said liver basement membrane composition. Claim 19 is directed to a collagenous tissue graft structure comprising decellularized basement membrane wherein DNA content of the basement membrane is about 0.566 to about 0.04 ug/mg dry weight of the basement membrane.

Badylak teaches a tissue graft composition comprising liver basement membrane prepared by removing the cellular components from liver tissue by treating the liver tissue with a solution comprising an enzyme, such as trypsin or pepsin, and a calcium chelating agent or chaotropic agent such as a mild detergent Triton 100, or with a solution comprising only the chelating agent or chaotropic agent (e.g. abstract, column 3, lines 1-15). The liver tissue slice can be suspended in an agitated solution containing protease, optionally containing a chaotropic agent or a calcium chealating agent in an amount effective to optimize release and separation of cells from the basement membrane without substantial degradation of the membrane matrix (e.g. column 3, lines 16-24). Badylak further teaches that the liver basement membrane can be

fluidized or in powder form (e.g. column 3, lines 39-60, column 11, 12), cell growth substrate are formed from fluidized forms of liver basement membrane and the fluidized tissue can be gelled to form solid or semi-solid matrix (e.g. column 8, lines 12-18), and the cell growth substrate can be combined with nutrients, such as minerals, amino acids, sugars, peptides, proteins, glycoproteins that facilitate cellular proliferation and growth factors (e.g. column 8, lines 26-32). Badylak also teaches that "fluidized forms of liver basement membrane can be used to coat culture-ware with a matrix comprising liver basement membrane devoid of source liver tissue endogenous cells. Thus, liver basement membrane can be used as a cell growth substrate in a variety of forms, including a sheet-like configuration, as a gel matrix, as an additive for art-recognized cell/tissue culture media, or as coating for culture-ware to provide a more physiologically relevant substrate that support and enhances the proliferation of cells" (e.g. column 7, lines 48-53). Since the specification fails to disclose any basement membrane having the DNA content recited in the claim (see the new matter rejection set forth above), it appears that the claimed decellularized basement membrane or liver basement membrane is isolated from a subject without any exogenous modification. It is inherent that the liver basement membrane isolated by Badylak contains the DNA content recited in the claim. Thus, claims 11-15 and 17-19 are anticipated by Badylak.

8. Claims 11-15 and 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Badylak, Stephen, 1998 (WO 98/25637).

Claims 11-15, 17 and 18 are directed to a purified liver basement membrane graft composition comprising basement membrane of warm-blooded vertebrate liver tissue, wherein

the DNA content of the liver basement membrane is about 0.566 to about 0.04 microgram of DNA per milligram of dry weight of the liver basement membrane, and wherein the liver basement membrane could be fluidized, in gel form, or in powder form, and a liver tissue derived composition for supporting the growth of a cell population, said composition comprising said liver basement membrane composition and is devoid of source liver tissue endogenous cells, or said composition comprising culture-ware coated with a matrix comprising said liver basement membrane composition. Claim 19 is directed to a collagenous tissue graft structure comprising decellularized basement membrane wherein DNA content of the basement membrane is about 0.566 to about 0.04 ug/mg dry weight of the basement membrane.

Badylak teaches a tissue graft composition comprising liver basement membrane prepared by removing the cellular components from liver tissue by treating the liver tissue with a solution comprising an enzyme, such as trypsin or pepsin, and a calcium chelating agent or chaotropic agent such as a mild detergent Triton 100, or with a solution comprising only the chelating agent or chaotropic agent (e.g. abstract, p. 3-4). The liver tissue slice can be suspended in an agitated solution containing protease, optionally containing a chaotropic agent or a calcium chealating agent in an amount effective to optimize release and separation of cells from the basement membrane without substantial degradation of the membrane matrix (e.g. p. 4). Badylak further teaches that the liver basement membrane can be fluidized or in powder form (e.g. p. 4-5, 16), cell growth substrate are formed from fluidized forms of liver basement membrane and the fluidized tissue can be gelled to form solid or semi-solid matrix (e.g. p. 11, second paragraph), and the cell growth substrate can be combined with nutrients, such as minerals, amino acids, sugars, peptides, proteins, glycoproteins that facilitate cellular

proliferation and growth factors (e.g. p. 11, third paragraph). Badylak also teaches that "fluidized forms of liver basement membrane can be used to coat culture-ware with a matrix comprising liver basement membrane devoid of source liver tissue endogenous cells. Thus, liver basement membrane can be used as a cell growth substrate in a variety of froms, including a sheet-like configuration, as a gel matrix, as an additive for art-recognized cell/tissue culture media, or as coating for culture-ware to provide a more physiologically relevant substrate that support and enhances the proliferation of cells" (e.g. p. 10, 2nd paragraph). Since the specification fails to disclose any basement membrane having the DNA content recited in the claim (see the new matter rejection set forth above), it appears that the claimed decellularized basement membrane or liver basement membrane is isolated from a subject without any exogenous modification. It is inherent that the liver basement membrane isolated by Badylak contains the DNA content recited in the claim. Thus, claims 11-15 and 17-19 are anticipated by Badylak.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.
/Shin-Lin Chen/

Primary Examiner, Art Unit 1632